

Summary:

Horizontal gene transfers link a human MRSA pathogen to contagious bovine mastitis bacteria

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Methicillin-resistant *Staphylococcus aureus* (MRSA) is a significant and growing worldwide public health threat. We provide DNA-evidence that many virulence factor genes in the human epidemic EMRSA-16 strain originated from different causative agents of contagious bovine mastitis. The DNA exchanges include genes that enable survival in deep-tissue abscesses and promote secretion of toxins. Initially identified as the cause of a 1991 hospital outbreak within the East Northamptonshire district of the United Kingdom, EMRSA-16 has spread globally to become one of the most clinically important hospital-acquired epidemic MRSA pathogens.

Using a newly developed web-accessible computer program (*EvoPrinter*), we have identified 16 different DNA regions within the EMRSA-16 genome that are present in contagious bovine mastitis bacteria but are not found in any of the other human *Staphylococcus* isolates that have been characterized thus far. EMRSA-16 uniquely shares 14 different DNA sequence blocks with the bovine mastitis *Staphylococcus aureus* ET3 pathogenic strain. Among dairy herds, *Staphylococcus aureus* is one of the major causal agents of contagious bovine mastitis. Our studies also reveal that EMRSA-16 has acquired virulence factor genes from other bovine mastitis bacteria pathogens. For example, one of the EMRSA-16 unique DNA regions (3,143 base-pairs) shares 99.8% nucleotide identity with two *Listeria monocytogenes* genes that encode factors that are involved in resistance to metal toxicity.

The finding of unique virulence factor genes in a human epidemic MRSA pathogen whose potential sources are bacteria that cause bovine mastitis, including *Staphylococcus aureus*, *Staphylococcus saprophyticus* and *Listeria monocytogenes*, suggests that there may be a common epidemiological association between these pathogens and that co-infections in cows and/or humans are a likely point of origin for these exchanges. Taken together, our observations suggest that gene transfers between human and livestock bacteria may be more prevalent than previously recognized and animal husbandry practices that enhance the possibility of human-livestock bacterial co-infections should be avoided. Further work is required to comprehend the full import of these exchanges and to understand their public health ramifications.

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